Appl Serial No.: 10.068,965

Attorney Docket No.: DCLERC-2P1

Reply Dated October 2 2003

This listing of claims will replace all prior versions, and listings, of claims in the application:

## **Listing of Claims:**

1-37. (Cancelled)

- 38. (New) A pharmaceutical composition for modulating angiogenesis comprising a therapeutically effective amount of an angiogenesis modulating compound and a pharmaceutically acceptable excipient, wherein said modulating compound is a recombinant caveolin-1, a nucleic acid encoding the partial or total amino acid sequence of caveolin-1, or a pharmacologically acceptable derivative thereof or an analogue thereof.
- 39. (New) The composition of claim 38, wherein said modulating compound is a recombinant caveolin-1 or a pharmacologically acceptable derivative thereof.
- 40. (New) The composition of claim 38, wherein said modulating compound is a nucleic acid encoding the partial or total amino acid sequence of caveolin-1, or an analogue thereof.
- 41. (New) The pharmaceutical composition of claim 40, wherein said nucleic acid is comprised in a recombinant expression vector.
- 42. (New) A pharmaceutical composition for modulating angiogenesis comprising a therapeutically effective amount of an angiogenesis modulating compound and a pharmaceutically acceptable excipient, wherein said modulating compound is a nucleic acid modulating the expression of caveolin-1.
- 43. (New) A pharmaceutical composition for modulating angiogenesis comprising a therapeutically effective amount of an angiogenesis modulating compound and a pharmaceutically acceptable excipient, wherein said modulating compound influences the translation or stability of caveolin-1 mRNA.

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44. (New) The pharmaceutical composition of claim 43, wherein said compound is an antisense nucleic acid which hybridizes with a sequence encoding the partial or total amino acid sequence of caveolin-1.

- 45. (New) The pharmaceutical composition of claim 44, wherein said antisense nucleic acid is comprised in a recombinant expression vector.
- 46. (New) The pharmaceutical composition of claim 44, wherein said antisense nucleic acid is SEQ ID NO:5.
- 47. (New) A pharmaceutical composition for modulating angiogenesis comprising a therapeutically effective amount of an angiogenesis modulating compound and a pharmaceutically acceptable excipient, wherein said modulating compound is an agonist of caveolin-1, an antagonist of caveolin-1, or a competitive inhibitor of caveolin-1.
- 48. (New) The pharmaceutical composition of claim 47, wherein said inhibitor is a scavenging or trapping molecule.
- 49. (New) The pharmaceutical composition of claim 48, wherein said scavenging or trapping molecule traps endogenous caveolin-1.
- 50. (New) The pharmaceutical composition of claim 49, wherein said molecule comprises the amino acid sequence of SEQ ID NO:4.
- 51. (New) The pharmaceutical composition of claim 49, wherein said molecule comprises one of the amino acid sequences of SEQ ID NOS:6-86.
- 52. (New) The pharmaceutical composition of claim 48, wherein said scavenging or trapping molecule traps endogenous eNOS mimicking the caveolin-1 molecule.

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54. (New) A pharmaceutical composition for modulating angiogenesis comprising a therapeutically effective amount of an angiogenesis modulating compound and a pharmaceutically acceptable excipient, wherein said modulating compound is a recombinant hsp90, a nucleic acid encoding the partial or total amino acid sequence of hsp90 or a pharmacologically acceptable derivative thereof or an analogue thereof.

- 55. (New) The pharmaceutical composition of claim 54, wherein said modulating compound is a recombinant hsp90, or a pharmacologically acceptable derivative thereof.
- 56. (New) The pharmaceutical composition of claim 54, wherein said modulating compound is a nucleic acid encoding the partial or total amino acid sequence of hsp90 or an analogue thereof.
- 57. (New) The pharmaceutical composition of claim 56, wherein said nucleic acid is comprised in a recombinant expression vector.
- 58. (New) A pharmaceutical composition for modulating angiogenesis comprising a therapeutically effective amount of an angiogenesis modulating compound and a pharmaceutically acceptable excipient, wherein said modulating compound is a nucleic acid modulating the expression of hsp90.
- 59. (New) A pharmaceutical composition for modulating angiogenesis comprising a therapeutically effective amount of an angiogenesis modulating compound and a pharmaceutically acceptable excipient, wherein said modulating compound influences the translation or stability of hsp90 mRNA.
- 60. (New) The pharmaceutical composition of claim 59, wherein said compound is an antisense nucleic acid which hybridizes with a sequence encoding the partial or total amino acid sequence of hsp90.

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62. (New) A pharmaceutical composition for modulating angiogenesis comprising a therapeutically effective amount of an angiogenesis modulating compound and a pharmaceutically acceptable excipient, wherein said modulating compound is a agonist of hsp90, an antagonist of hsp90, or a competitive inhibitor of hsp90.

- 63. (New) The pharmaceutical composition of claim 62, wherein said inhibitor is a scavenging or a trapping molecule.
- 64. (New) A composition comprising a statin and hsp90 or a pharmacologically acceptable derivative thereof as a combined preparation for simultaneous, separate or sequential use in a therapy in an angiogenesis-related disease.
- 65. (New) A composition comprising a growth factor and hsp90 or a pharmacologically acceptable derivative thereof as a combined preparation for simultaneous, separate or sequential use in a therapy in an angiogenesis-related disease.
- 66. (New) A medicament for the modulation of proangiogenic actions of a statin and/or a growth factor comprising hsp90 or a pharmacologically acceptable derivative thereof.
- 67. (New) A method of modulating angiogenesis comprising trapping endogenous caveolin-1 by a trapping compound thereby preventing its binding to the endothelial isoform nitric oxide synthase (eNOS).
- 68. (New) The method according to claim 67, wherein said trapping compound comprises the amino acid sequence of SEQ ID NO:4, preferably comprising the amino acid sequence pattern as described in SEQ ID NO 6 to SEQ ID NO 86.
- 69. (New) The method according to claim 67, wherein said trapping compound comprises one of the amino acid sequences of SEQ ID NOS:6-86.

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70. (New) A method of modulating angiogenesis comprising trapping endogenous eNOS by a trapping compound wherein said trapping compound mimicks caveolin-1.

- 71. (New) The method according to claim 70, wherein said trapping compound comprises the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:3.
- 72. (New) A method of modulating angiogenesis comprising overexpressing or improving the activity of caveolin-1 or hsp90.
- 73. (New) A method of modulating angiogenesis comprising reducing the abundance and/or activity of caveolin-1 or hsp90.
- 74. (New) A method for the treatment of an angiogenesis related disease comprising administering a therapeutically effective amount of an angiogenesis modulating compound to an individual in need thereof, wherein said modulating compound is a recombinant of caveolin-1, a nucleic acid encoding the partial or total amino acid sequence of caveolin-1, or an analogue thereof or a pharmacologically acceptable derivative thereof, a compound modulating the expression of caveolin-1, an agonist or an antagonist or a competitive inhibitor of caveolin-1, a recombinant hsp90, a nucleic acid encoding the partial or total amino acid sequence of hsp90 or an analogue thereof or a pharmacologically acceptable derivative thereof, a compound modulating the expression of hsp90, an agonist or an antagonist or a competitive inhibitor of hsp90.
- 75. (New) The method according to claim 74 wherein said angiogenesis related disease is angiogenesis dependent tumour growth and metastatic disease, ischemic heart and peripheral vascular disease including cerebral diseases and wound healing.
- 76. (New) A diagnostic kit for testing a compound or a composition for the ability to modulate angiogenesis comprising an angiogenesis modulating compound wherein said modulating compound is a recombinant of caveolin-1, a nucleic acid encoding the partial or

agonist of an antagonist of a competitive inhibitor of caveolin-lia recombinant hsp90, a

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nucleic acid encoding the partial or total amino acid sequence of hsp90 or an analogue thereof or a pharmacologically acceptable derivative thereof, a compound modulating the expression of hsp90, an agonist or an antagonist or a competitive inhibitor of hsp90.

- 77. (New) A pharmaceutical composition for modulating angiogenesis comprising a therapeutically effective amount of an angiogenesis modulating compound and a pharmaceutically acceptable excipient, wherein said modulating compound is a recombinant polypeptide from the cholesterol-caveolin1-eNOS-NO pathway or the mevalonate pathway, a nucleic acid encoding the partial or total amino acid sequence of said polypeptide, or a pharmacologically acceptable derivative thereof or an analogue thereof.
- 78. (New) The pharmaceutical composition of claim 45, whereby said antisense nucleic acid is SEQ ID NO:5.